# Evaluation of dynamic weight bearing (gait) following unilateral sciatic nerve crush in the mouse

NEUROFIT PRECLINICAL RESEARCH

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## Introduction

Sciatic nerve crush in the mouse is a widely used animal model for peripheral nerve injury / regeneration. Improved walking gait as assessed by the analysis of paw print parameters is often used as functional assessment to indicate axonal regeneration. However, full recovery in walking gait is observed within 2-3 weeks following mouse sciatic nerve crush injury * despite poor electromyography and histomorphometry outcomes.

It has been noted after sciatic nerve crush that mice often refrain from putting full weight on the affected limb and keep it sometimes in an elevated position. This phenomenon is not observed in sham-operated animals and thus suggests that weight bearing deficit in mouse nerve crush model is most plausibly of neuropathic origin.

*, Brain Res. 2002;943(2):283-6 ; J Cell Biol. 2002;159(1):29-35.

## Materials and Methods

### Sciatic nerve crush model :

Male CD-1 mice are subject to sciatic nerve crush at the mid-thigh level.
For sham operated animals, sciatic nerves are exposed but not crushed.

#### Measure of hind limb weight bearing in the mouse

The animals' weight distribution on the four limbs is assessed using an incapacitance tester. Weight bearing deficit is evaluated through the ipsi / contralateral hindpaws weight ratio.

#### Measure of Compound Muscle Action Potential (CMAP)

The amplitude of CMAP is measured in the right gastrocnemius muscle (ipsilateral) of in anaesthetized mice using subcutaneous monopolar needle electrodes. Stimulation is performed at the right sciatic notch using supramaximal (12.8 mA) square waves pulses of 0.2 ms duration.

#### Histomorphometry of nerve fibers

Axon size and g-ratio (relative myelin sheath thickness) are evaluated from transversal sections of eppon-embedded tibial nerves.

## Objectives

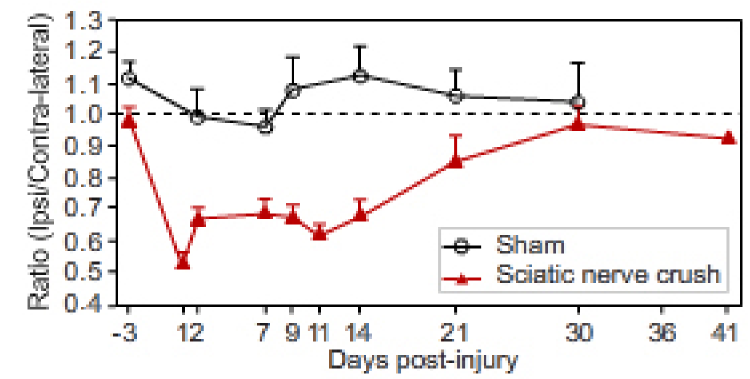
The aim of the present study is:

- to assess whether weight bearing deficit can be easily monitored after sciatic nerve crush in the mouse
- to establish the time course of the dysfunction
- and to draw potential correlations between weight bearing deficit and electrophysiological and histomorphometric changes.

## Results

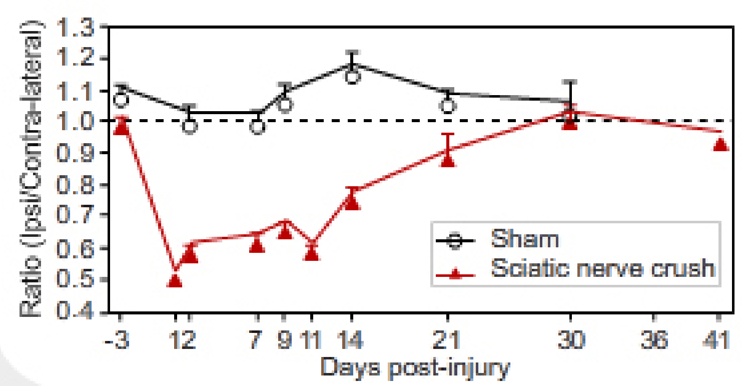
**Measure of weight distribution is readily achievable in the sciatic nerve crush model and does not require any specific expertises.**

**Figure 1a** : Weight bearing ratio of rear paws



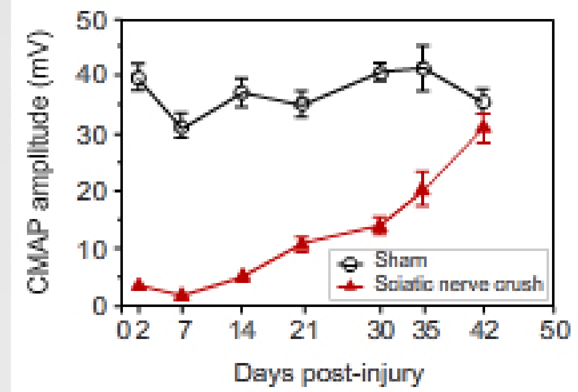

Graphs showing gait dysfunction as assessed by the measure of weight distribution on the hind limbs of the mouse following sciatic nerve crush.

**Figure 1b** : Surface bearing ratio of rear paws

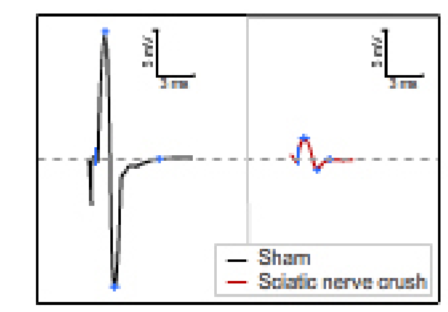



Note that the dysfunction remains very pronounced 2 weeks after the nerve crush and full recovery is observed between week 4 and 6 post-crush.

**Figure 2** : Electromyography




Time course of change in the amplitude of CMAP following sciatic nerve crush.




Representative diagram of CMAP recorded in sham-operated and nerve crushed mice at Day 2 post-surgery.

**Figure 3** : Nerve morphometry

Graph showing the disruption of g-ratio and fibers size profile in tibial nerve following a sciatic nerve crush.

(4 weeks post-injury)

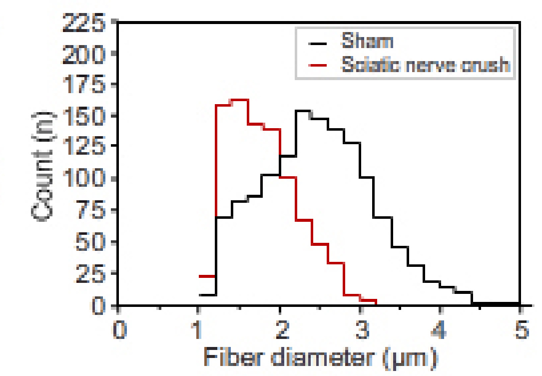



**Figure 4** : Histology


SHAM: Representative tibial nerve section of sham-operated mice. Note the presence of matured axons surrounded by well defined myelin sheath.

CRUSH Day 2: Complete destruction of myelinated fibers. Note the presence of thin myelin sheath surrounding fairly large empty space left by a degenerated axon.

CRUSH Week 1: Presence of numerous degenerating myelins and premises of regenerating myelinated axons (small caliber axon ensheathed by schwann cells).

CRUSH Week 2: Similar observation as in Week 1.

CRUSH Week 4: Disappearance of myelin debris and clearance processes. Presence of numerous small caliber myelinated axons and axons ensheathed by schwann cells. Note the absence of debris clearance process.

## Summary of key findings

- Longitudinal follow-up measurement of weight bearing deficit can be easily monitored in the mouse sciatic nerve crush model
- Full recovery from weight bearing deficit occurred between 4-6 weeks post-injury
- Full recovery in weight distribution coincides with the disappearance myelin debris clearance process along with presence of numerous regenerated axons
- Full recovery in weight distribution is observed whilst CMAP amplitude and axon size only show 40% recovery.